UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/030,571	02/24/1998	CHARLES R. CANTOR	25491-2401G	7542

20985 7590 07/14/2005

FISH & RICHARDSON, PC
12390 EL CAMINO REAL
SAN DIEGO, CA 92130-2081

EXAMINER	
FORMAN, BETTY J	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/030,571	CANTOR ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *70,72-79,92-94,123,124,127-133 and 135-139* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *70,72-79,92-94,123,124,127-133 and 135-139* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. This action is in response to papers filed 3May 2005 in which a Supplemental Information Disclosure Statement was submitted, claims 74, 76, 127, 132 and 133 were amended and claim 139 was added. The amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 3 November 2004, not reiterated below, are withdrawn in view of the amendments. The previous office action indicated allowability of Claims 127-133 and 135-138. However, Claim 127 has been amended. Upon reconsideration of the amended claims in view of the IDS, the claims are no longer deemed free of the prior art.

Applicant's arguments have been thoroughly reviewed and are discussed below as they apply to the instant grounds for rejection. New grounds for rejection, necessitated by the amendments and IDS, are discussed.

Claims 70, 72-79, 92-94, 123-124, 127-133 and 135-139 are under prosecution.

Information Disclosure Statement

2. The references received 3 May 2005 have been reviewed as indicated on the initialed 1449. The references lined-through have not been considered because they are non-English language documents. Applicant's state that the non-English language documents are provided with the English language equivalent PCTs. The PCTs have been reviewed for their content as noted by the initialed 1449.

Claim Rejections - 35 USC § 112

35 U.S.C. 112: First paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 70, 72-73 and 77-79 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

a. The recitation "wherein the variable sequence is not at the 5' terminus or 3' terminus" is added to the newly amended independent claim 70 (from which Claims 72, 73, 77-79 depend). However, the specification fails to define or provide any disclosure to support such claim recitation.

Response to Arguments

5. Applicant points to pages 6, 27 and 56 for a teaching of the random sequence at the probe terminus and further page 6 for a teaching of the random sequence within the single stranded portion. Applicant asserts that because the specification provides two alternative embodiments, one of ordinary skill in the art would recognize that applicant had possession of a random sequence at the terminus or contained within the single-stranded region. Applicant further asserts that because alternative embodiments are positively recited in the specification, they may be explicitly excluded in the claims.

The arguments have been considered but are not found persuasive. As Applicant notes, the courts have stated that positively recited alternative embodiments may be explicitly excluded in the claims (see below, MPEM § 2173.05(i)).

> Any negative limitation or exclusionary proviso must have basis in the original disclosure. If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. See In re Johnson, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977) ("[the] specification, having described the whole, necessarily described the part remaining."). See also Ex parte Grasselli, 231 USPQ 393 (Bd. App. 1983), aff'd mem., 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

However, in the instant case, alternative embodiments are not positively recited. While the specification teaches a random sequence at the 5' or 3' terminus and further teaches the random sequence within the single stranded region, it is unclear that the specification is teaching alternative embodiments. An exemplary example of alternative embodiments would recite the embodiments explicitly within a single passage as A, B or C. The specification does not contain such a recitation. In contrast, the specification provides generalized descriptions of the random sequence in different passages of the specification. It is unclear from the specification whether the cited passages are describing alternative embodiments for random sequence position because the term "within" encompasses the termini. Furthermore, because the term "sequence" encompasses more than one nucleotide, a random sequence at the termini would have one nucleotide at the termini while the remaining portion of the randomness would be upstream of the termini i.e. within the single-stranded portion. Therefore, in contrast to alternative embodiments, the specification teaches a random sequence at the 3' or 5' termini having a random sequence within the single stranded portion. As such, the embodiments described in the specification are not positively recited alternative embodiments.

Nowhere in the cited passages, or specification as a whole, is the random sequence defined as excluding the termini as claimed. Hence, the amendments discussed above constitute new matter.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 70, 72, 74, 76-79, 92-94, 124 and 136 are rejected under 35 U.S.C. 102(e) as being anticipated by Deugau et al (U.S. Patent No. 5,508,169, filed 6 April 1990).

Regarding Claim 70, Deugau et al disclose an array of nucleic acid probes (i.e. complete panel of indexing linkers) wherein each probe has a double-stranded portion and a terminal single stranded portion comprising a variable nucleotide sequence within the single-stranded portion (Column 11, lines 14-25, Fig. 2 and Claim 33). Furthermore, Deugau et al the Type IIS enzymes used to produce the single-stranded regions produce "any of the possible permutations and combinations of nucleotides" (Column 10, lines 14-18). Hence, the single stranded regions are not produced with any order, but are instead, random. Furthermore, the random portions are within the single-stranded regions as defined in the instant specification.

Additionally, because the single stranded portion of Deugau et al has a terminal nucleotide and the number of nucleotides between the terminal nucleotide and the double stranded portion of the probe varies providing a random single stranded sequence that would be interpreted as being not at the terminus, but instead between the terminus and the double stranded portion.

The courts have stated that claims must be given their broadest reasonable interpretation consistent with the specification *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997); *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969); and *In re Zletz*, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) (see MPEP 2111). Given the broadest reasonable interpretation in view of the claim language and specification, Deugau et al teach the probes as claimed.

Regarding Claim 72, Deugau et al disclose the array wherein the double-stranded portion (i.e. common sequence # 1026, # 1504 and # 1701) is between about 3-20 nucleotide and the single stranded portion is between about 3-20 nucleotides (Columns 15-16, Table I and Table II).

Regarding Claim 74, Deugau et al teach an array of probes comprising a first nucleic acid hybridized to the second nucleic acid forming a hybrid having a double-stranded portion and a single-stranded portion (Column 11, lines 14-25; Columns 15-16, Table I and Table II; Fig. 2; and Claim 33).

Furthermore, Deugau et al the Type IIS enzymes used to produce the single-stranded regions produce "any of the possible permutations and combinations of nucleotides" (Column 10, lines 14-18). Hence, the single stranded regions are not produced with any order, but are instead, random.

The courts have stated that patentability of a product is based on the product, not method of making the product. Because Deugau et al teach the product i.e. array of probes, the disclose the instantly claimed array.

> "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is **based on the product itself**. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different

process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) see MPEP 2113.

Regarding Claim 76, Deugau et al teach the array wherein the solid support is a two-dimensional matrix with multiple probe binding sites i.e. the probes are attached to spatially segregated solid phase substrates (Column 10, lines 45-51).

Regarding Claim 77, Deugau et al teach the array wherein the probes are labeled with a detectable label (Claim 27).

Regarding Claim 78, Deugau et al teach the array wherein the label comprises a radioisotope or fluorescent chemical (Claims 27 & 28).

Regarding Claim 79, Deugau et al teach the array wherein the nucleic acids are DNA (Claims 25 and 33).

Regarding Claim 92, Deugau et al teach the array wherein the probes are labeled with a detectable label (Claim 27).

Regarding Claim 93, Deugau et al teach the array wherein the label comprises a radioisotope or fluorescent chemical (Claims 27 & 28).

Regarding Claim 94, Deugau et al teach the array wherein the nucleic acids are DNA (Claims 25 and 33).

Regarding Claim 124, Deugau et al teach the array comprising about 4^r different nucleic acid probes (i.e. complete panel of indexing linkers) (Column 11,lines 14-25).

Regarding Claim 136, Deugau et al teach the array wherein the constant portion includes an enzyme restriction site (Column 6, lines 1-21).

Response to Arguments

8. Applicant argues that Deugau et al dose not teach a probe having a random sequence not at the terminus. The argument has been considered. However, as stated above, the specification defines the instant probes as having the random sequence within the single-stranded region. Therefore, Deugau et al teach the probes as defined in the specification.

Applicant asserts that the instantly claimed random sequences as defined by the specification are of a specified length and further asserts that the specification does not define random as encompassing varied length as described in the rejection above. The argument has been considered but is not found persuasive because the claims are not limited to the preferred embodiment as asserted. The claims merely require a random sequence. The claims do not define or limit the randomness of the sequence. Therefore, the argument is not commensurate in scope with the claims.

Applicant argues that Deugau does not teach an invariable nucleotide at the termini and therefore does not teach the claimed probes. The argument has been considered but is not found persuasive. The claims are drawn to a random sequence. As stated above, Deugau teaches a random sequence within the single stranded portion and between the termini and double-stranded portion as claimed.

Applicant argues that Deugau et al does not teach the probes as define in Claim 74 wherein an oligonucleotide is ligated to the random sequence providing a single-stranded region of 7 to 30 nucleotides. The argument has been considered but is not found persuasive because the argument is not commensurate in scope with the claims. In contrast to Applicant's assertion, the claims do not require a single-stranded region of 7 to 30 nucleotides. The claims are drawn to a first sequence of **about** 15-25 hybridized to a second, longer sequence of **about** 20-30 wherein the longer sequence is ligated to a oligo of **about** 4 to 20 nucleotides producing a single-stranded portion random region of **about** 3-10 nucleotides. There are many examples whereby the probe does not have a single-stranded region of 7 to 30 nucleotides as asserted. For example, if the first sequence comprises 25 nucleotides, the second sequence is 26 wherein the last 2 (about 3) are random and the oligo is 3 (about 4), ligation of the oligo to the second nucleotide provides a single stranded random region of 5. Deugau teaches a single-stranded region of 5 nucleotides (Column 9, lines 28-33). This is but one of the many combinations encompassed by the teaching of Deugau.

NEW GROUND FOR REJECTION

9. Claims127-133, 135-139 are rejected under 35 U.S.C. 102(b) as being anticipated by Hornes et al (WO 90/06045, published 14 June 1990).

Regarding Claim 127, Hornes et al disclose a array of probe wherein each probe comprises a single-stranded portion comprising a variable region (non-hybridized target) and a double-stranded portion (oligo-dT) wherein the probes are divide into four subsets wherein each subset a nucleic acid base occupies a defined number of positions (e.g. biotinylated nucleotide at the end, page 8, lines 7-11 or incorporated ddNTP, page 14, lines 1-15) and all other bases (non-biotinylated A, T, C, G) occupy the remaining positions (page 15, lines 15-35).

Regarding Claims 138 and 128, Hornes et al disclose the array wherein the probes are fixed to a solid support via a coupling agent e.g. biotin (page 8, lines 7-11 and page 11, lines 23-26).

Regarding Claim 129, Hornes et al disclose the array wherein the probes are labeled (page 15, lines 15-35).

Regarding Claim 130, Hornes et al disclose the array wherein the label is a radioisotope or fluorescent molecule (page 13, line22-page 14, line 29).

Regarding Claim 131, Hornes et al disclose the array wherein the nucleic acids are DNA or RNA (page 2, lines9-22).

Regarding Claim 132, Hornes et al disclose the array wherein the solids support is metal (page 4, lines 14-35).

Regarding Claim 133, Hornes et al disclose the array wherein the solid support is three-dimensional having multiple binding sites (page 5, line 19-page 7, line 9).

Regarding Claim 135, Hornes et al disclose the array wherein the non-fixed positions are occupied by analoges i.e. the fixed nucleotide is the biotinylated nucleotide at the end, page 8, lines 7-11 and the non-fixed positions if the incorporated ddNTP (page 14, lines 1-15).

Regarding Claim 136, Hornes et al disclose the array wherein the double stranded portion includes a restriction site (page 18, lines 32-37).

Regarding Claims 137, Hornes et al disclose the array wherein the probes are fixed to a solid support via a coupling agent e.g. biotin (page 8, lines 7-11 and page 11, lines 23-26).

Regarding Claims 138, Hornes et al disclose the array wherein the probes are fixed to a solid support via a coupling agent e.g. biotin (page 8, lines 7-11 and page 11, lines 23-26).

Regarding Claims 139, Hornes et al disclose the array wherein the probes are fixed to a solid support via a coupling agent e.g. biotin (page 8, lines 7-11 and page 11, lines 23-26).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claim 73, 123 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deugau et al (U.S. Patent No. 5,508,169, filed 6 April 1990) in view of Brenner et al (Proc. Natl. Acad. Sci. USA, 1989, 86: 88902-8906).

Regarding Claims 73, 123, Deugau et al disclose the array of nucleic acid probes (i.e. complete panel of indexing linkers) wherein each probe has a double-stranded portion at the 3' terminus, a single stranded portion at the 5' terminus and a random nucleotide sequence of length R within the single-stranded portion (Column 11, lines 14-25, Fig. 2 and Claim 33) wherein the probes are immobilized to a solid support (Column 11, lines 14-25) but they do not specifically teach the means by which the probes are immobilized. However, coupling agents e.g. biotin/streptavidin immobilization was well known in the art at the time the claimed

invention was made as taught by Brenner et al who teach that biotin/streptavidin provides a versatile means of capture immobilization (page 8904, second full paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the biotin/streptavidin of Brenner et al to the immobilization of Deugau et al based on the teaching of Brenner et al to thereby provide versatile capture immobilization (page 8904, second full paragraph).

Response to Arguments

12. Applicant states that Deugau et al does not teach an array of probes comprising a random sequence not at the terminus. The argument has been considered but is not found persuasive. As stated above, Deugau et al teach the single-stranded portion is random. Hence, Brenner is not relied upon for this element. Applicant further argues that Brenner does not cure the deficiencies of Deugau because they do not teach a random sequence not at the termini. The argument has been considered but is not found persuasive for the reasons stated above.

13. Claim 75 is rejected under 35 U.S.C. 103(a) as being unpatentable over Deugau et al (U.S. Patent No. 5,508,169, filed 6 April 1990) in view of Ghosh et al (Nucleic Acids Research, 1987, 15: 5353-5372).

Regarding Claim 75, Deugau et al teach an array of probes comprising a first nucleic acid hybridized to the second nucleic acid forming a hybrid having a double-stranded portion and a single-stranded portion (Column 11, lines 14-25; Columns 15-16, Table I and Table II; Fig. 2; and Claim 33). Wherein the probes are fixed to a solid support as taught by Ghosh et al (Column 10, lines 45-51 and Claim 26) but they do not specifically teach the material from

which the solid support is made. However, Ghosh et al teach their solid support is selected from plastics and resins (page 5356, first full paragraph-page 5357, last paragraph).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the solid supports of Ghosh et al to the immobilization of Deugau et al and to immobilize the probes onto plastic or resin support based on the suggestion of Deugau et al (Column 10, lines 45-51 and Claim 26) thereby utilizing well known supports for the expected benefits of successful immobilization.

Response to Arguments

14. Applicant states that Deugau et al does not teach an array of probes comprising a random sequence not at the terminus. The argument has been considered but is not found persuasive as discussed above.

15. Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 3 May 2005 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609(B)(2)(i). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

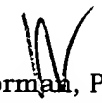
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.



BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
July 13, 2005